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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/884,873	06/30/1997	PHILLIP DAN COOK	ISIS-2202	6678

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EXAMINER

BAKER, MAURIE GARCIA

ART UNIT	PAPER NUMBER
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1639
DATE MAILED: 06/30/2003

37

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 08/884,873	Applicant(s) Cook
Examiner Maurie G. Baker, Ph.D.	Art Unit 1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on Apr 10, 2003

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) Claim(s) 2-5, 7-12, and 33 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 2-5, 7-12, and 33 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892)

4) Interview Summary (PTO-413) Paper No(s). _____

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) Notice of Informal Patent Application (PTO-152)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

6) Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.
2. The amendment filed April 10, 2003 (Paper No. 35) has been entered. In this paper, claim 33 was amended. Currently, claims 2-5, 7-12 and 33 are pending.
3. There was a previous restriction requirement and species election in the instant case. As per MPEP§ 818.02(a), the previous election carries over to prosecution in this continued examination case (“[t]he claims originally presented and acted upon by the Office on their merits determine the invention elected by an applicant in the application, and in any request for continued examination (RCE) which has been filed for the application.”).
4. The previously elected species contained a pyrimidine scaffold structure (elected mixture was encompassed by structure I). *Structure I has now been removed from claim 33 via amendment.* Thus, the search has been expanded to non elected species at the examiner’s discretion. Please see MPEP § 803.02 “should no prior art be found that

anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. **The prior art search, however, will not be extended unnecessarily to cover all nonelected species”.**

Status of Rejections

5. The previous rejection under 35 U.S.C. 112, second paragraph is withdrawn in view of applicant's arguments. The previous rejection under 35 U.S.C. 103(a) is withdrawn in view of applicant's claim amendments. New rejections over the claims *as amended* are set forth below.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5, 7, 8, 10, 11, 12 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The independent claim 33 has been substantially amended over the course of prosecution. As a result of these amendments, dependent claims 5, 7, 8, 10, 11 and 12 are confusing for the following three reasons:

(1) Claims 5 and 7 refer to said heterocyclic scaffold which “bears at least three functionalizable atoms” at least one of which is “nitrogen, oxygen or sulfur”. As the heterocyclic scaffolds are *specifically defined* as one of structures II or III (which have a set number and type of functionalizable atoms), dependent claims 5 and 7 are confusing. They appear to not limit, but broaden, the scope of the independent claim, which is improper.

(2) Claims 8 and 10 appear to be redundant in light of the requirements of claim 33. The claims require the situation where T and L must be present. However, it appears that claim 33, as currently amended, already has such a requirement. Thus claims 8 and 10 are confusing and appear to not further limit claim 33.

(3) Claims 11 and 12 appear to be duplicates of each other as claim 11 requires a T moiety, which is already required by claim 33 (see (2) above). Moreover, claims 11 and 12 do not appear to limit claims 10 and 33 (on which they depend) because they are product-by process claims. The patentability of a product does not depend on its method of production.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 2-5, 7-12 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Usbeck et al (JACS, 1961, Vol. 83, pp. 1113-1117) in view of Gordeev et al (WO 96/33972; of record) and Gordon et al (J. Med. Chem. 1994; of record).

Usbeck et al teach 8-triazenopurine nitrogen mustards that read on the claimed compounds having structure II (see page 1114, for example). These compounds are labeled “potential purine antagonists” and their biological activity is discussed (page 1113 and page 1115, 1st column, last paragraph). The triazenopurine compounds have least three functionalizable atoms on the purine scaffold (reading on instant claims 5 and 7). The compounds of the reference have groups that read on the claimed tethers, T where the tethers have least one functionalizable atom which is nitrogen, oxygen and/or sulfur and also on the claimed chemical substituents, L (reading on instant claims 8-10). Specifically considering the compounds of the reference in Tables I – III and page 1114, 2nd column of the reference, at least 10 compounds that read on the claimed structure II are shown. The compounds read on those claimed when j=1, e=0, T is O or NH and L is H for two of the T-L combinations and for the other T-L combination, T is -N=N- and L is N-dialkyl, aryl or thioalkyl. It is noted for the record that claims 11 and 12 appear to be product-by process claims. The patentability of a product does not depend on its method of production.

Usbeck et al lacks the teaching of specifically creating a *mixture* of at least 6 compounds.

However, Gordeev et al teach libraries of heterocyclic (pyrimidine) compounds, see Abstract. The library compounds of Gordeev et al have a heterocyclic scaffold (see page 34-35 and more specifically page 81) and are substantially homogeneous (page 35, bottom). The library compounds are made in a pooled format (see page 84, lines 18-28), for example, a pool of 21 pyrimidines is made and tested. This reads on the limitation of a mixture of at least 6 compounds and the further limitations of claims 2 and 3. All compounds are present in at least some of the pools and the compounds are synthesized at a purity (see page 81) where the mixture would be close to equimolarity, reading on the limitations of claim 4.

Also, Gordon et al teaches that “[w]hen small molecule leads for a target have been previously defined...the notion of searching for more potent derivatives among libraries combinatorially enriched in specific pharmacophore analogs is an obvious tactic to pursue” (page 1386 1st column, 1st full paragraph). Gordon et al additionally teaches the general principles of combinatorial chemistry and the rationale for creating libraries, see page 1385 and 1397-1401 generally. Specifically, the notion of intentional biasing as a form of drug design is taught (see page 1401, 1st column). Gordon et al teaches a “spectrum of molecular diversity” (see page 1397, Figure 19) that describes why a library of a certain size would be useful for a variety of different applications.

Therefore, it would have been *prima facie* obvious to one of ordinary skill to create a mixture (i.e. library) of six or more compounds of the claimed type

based on the teachings Usbeck et al as to the synthesis and uses of such compounds and the teachings of Gordeev et al and Gordon et al regarding libraries. A person of ordinary skill in the art would have been motivated to create libraries to have large numbers of molecules available for testing for improved properties (see Gordon, page 1398, 1st paragraph). A person of ordinary skill in the art would have been motivated to specifically create a mixture (i.e. pooled format) as Gordeev et al teaches the creation of libraries of heterocyclic compounds using this format.

Status of Claims/Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie Garcia Baker, Ph.D. whose telephone number is (703) 308-0065. The examiner is on an increased flextime schedule but can normally be reached on Monday-Thursday and alternate Fridays from 9:30 to 7:00.

12. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang, can be reached at (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie Garcia Baker, Ph.D.
June 27, 2003



MAURIE GARCIA BAKER PH.D
PRIMARY EXAMINER